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*Kelly A. Jones
Besa Smith
Nisara S. Granado
Edward J. Boyko
Gary D. Gackstetter
Margaret A.K. Ryan
Christopher J. Phillips
Tyler C. Smith*

for the Millennium Cohort Study Team



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*Naval Health Research Center
140 Sylvester Road
San Diego, California 92106-5321*

Newly Reported Lupus and Rheumatoid Arthritis in Relation to Deployment Within Proximity to a Documented Open-Air Burn Pit in Iraq

Kelly A. Jones, MPH, Besa Smith, MPH, PhD, Nisara S. Granado, MPH, PhD, Edward J. Boyko, MD, MPH, Gary D. Gackstetter, DVM, PhD, MPH, Margaret A.K. Ryan, MD, MPH, Christopher J. Phillips, MD, MPH, and Tyler C. Smith, MS, PhD; for the Millennium Cohort Study Team

Objective: To assess the relationship between possible exposure to smoke from documented open-air burn pits and newly reported lupus and rheumatoid arthritis among Millennium Cohort participants who have deployed in support of operations in Iraq and Afghanistan. **Methods:** Prospectively assessed self-reported lupus and rheumatoid arthritis among deployers who completed both 2004–2006 and 2007–2008 questionnaires. **Results:** After exclusions, more than 18,000 participants were deployed, including more than 3000 participants deployed within a 3-mile radius of a documented burn pit. After adjustment, proximity within 3 miles of a burn pit was not significantly associated with rheumatoid arthritis or lupus in general; however, one location was associated with lupus, although few cases were at this site ($n = 2$). **Conclusions:** Results indicate deployers potentially exposed to documented burn pits in the combined three-camp analysis were not at an elevated risk of lupus or rheumatoid arthritis.

Service members deploying in support of the operations in Iraq and Afghanistan may have higher odds of developing chronic diseases, such as lupus or rheumatoid arthritis, as a result of unique

From the Department of Deployment Health Research (Ms Jones, and Drs T. Smith, B. Smith, Granado, and Phillips), Naval Health Research Center, San Diego, Calif; Seattle Epidemiologic Research and Information Center (Dr Boyko), Department of Veterans Affairs Puget Sound Health Care System, Seattle, Wash; Analytic Services, Inc. (ANSER) (Dr Gackstetter), Arlington, Va; Occupational Health Department (Dr Ryan), Naval Hospital Camp Pendleton, Camp Pendleton, Calif; and Department of Community Health (Dr T Smith), School of Health and Human Services, National University, La Jolla, Calif.

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Address correspondence to: Kelly A. Jones, MPH, Naval Health Research Center, Deployment Health Research - Dept 164, 140 Sylvester Road, San Diego, CA 92106 (kelly.jones@med.navy.mil).

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exposures or a greater intensity of common exposures that have been associated with these diseases in the general US population.^{1–8} One such exposure suspected of contributing to illness, which is garnering much attention from media and veterans groups, is the burning of trash and other waste products in open-air burn pits.^{9–25} Although the range of chemicals released in these burn pit fires is unknown, analyses by the US Army Public Health Command suggest that toxins such as dioxins, polycyclic aromatic hydrocarbons, volatile organic compounds, carbon monoxide, hexachlorobenzene, and ash, among many others, may be generated from burning solid wastes.^{26–31} Some of these toxins are known carcinogens and a few, including pesticides, insecticides, heavy metals, silica dust, solvents, and others, have been implicated as potential autoimmune triggers in previous research.^{5,12–15,26,29,30,32,33} Also noted in a 2009 US Democratic Policy Committee hearing was the potential for short- and long-term health consequences because of harmful chemicals generated from slow, low-heat burning of trash, which have been associated with immune dysfunction, intelligence quotient deficit, and reproductive abnormalities.³⁴ Burn pit smoke contains substances that have been linked in previous research to autoimmune disorders, but whether the occurrence of autoimmune disorders differs by this exposure has not been previously investigated.

Autoimmune disorders are rare but together they affect approximately 5% to 8% of the general US population.^{35–37} Among military personnel, the prevalence of lupus and rheumatoid arthritis are lower, at 0.6% and 2.4%, respectively, possibly because of the younger average age of this population.³⁸ Previous investigation of newly reported lupus and deployment status among service members showed no association when compared with nondeployed, though a decreased risk of newly reported rheumatoid arthritis was found.³⁹ However, a more specific evaluation of deployment-related exposures, such as open-air burn pits, is needed.

We therefore prospectively examined the associations between proximity to documented open-air burn pits among service members deployed in support of the operations in Iraq and Afghanistan and the incidence of two of the more common autoimmune disorders (lupus and rheumatoid arthritis).

METHODS

Data Sources

The Millennium Cohort Study is a population-based study designed to prospectively investigate military service-related health concerns in all US service branches including active-duty and Reserve/National Guard members. The Millennium Cohort Study began collecting baseline data in July 2001, before the start of the current operations in Iraq and Afghanistan, and conducts follow-up assessment approximately every 3 years.^{40–42} Beginning in June 2004 and May 2007, follow-up data were collected for the first enrollment group, whereas baseline and follow-up data were respectively collected from the second enrollment group of the Cohort.

The Defense Manpower Data Center provided demographic, military characteristics, and deployment-related data, including a service member's proximity to a documented open-air burn pit within 2-, 3-, and 5-mile radii at three different campsites in Iraq between 2003 and 2008: Joint Base Balad (JBB), Camp Taji, and Camp Speicher. The burn pit located at JBB was the largest open-air burn pit located in US Central Command. Camp Speicher contained a burn pit area with seven individual open pits, whereas Camp Taji contained a large area with 20 documented open-air burn pits. These sites were used for solid waste disposal.

Electronic medical records were obtained from the Armed Forces Health Longitudinal Technology Application as well as the Medical Data Repository, whereas medication dispensed data were obtained from the Pharmacy Data Transaction System.

Lupus and Rheumatoid Arthritis

Newly reported lupus and rheumatoid arthritis were identified at baseline from the following question, "Has your doctor or other health professional ever told you that you have any of the following conditions?" At follow-up, participants were asked the same question, but in the context of "in the last 3 years." To ensure that each of the incident cases occurred after the potential burn pit exposure, newly reported disease was defined for the first enrollment group as an affirmative self-report of lupus or rheumatoid arthritis at follow-up (2007–2008) among participants not previously reporting the condition ever at baseline (2001–2003) or in the past 3 years at the first follow-up (2004–2006). The second enrollment participants had to positively endorse lupus or rheumatoid arthritis at the first follow-up (2007–2008) while also reporting no condition ever at baseline (2004–2006).

Case confirmation of newly reported lupus and rheumatoid arthritis was performed through review of electronic medical records. Lupus and rheumatoid arthritis cases were confirmed using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes (lupus: 710.0; rheumatoid arthritis: 714.0, 714.1, 714.2, 714.8, 714.9) and medications dispensed. Confirmed cases required at least one medication dispensed and at least one inpatient or outpatient medical encounter from the specified codes. In addition, detailed records of care for self-reported cases were reviewed, when available. These clinical reviews allowed inclusion of laboratory data, medications prescribed from nonmilitary sources, and all provider notes. Because of differential access to care among Reserve and National Guard members in the Department of Defense health care system, we restricted this review to active-duty participants who did not separate from the military.

Documented Open-Air Burn Pit Exposure

Documented open-air burn pit status was categorized as exposure within a 2-, 3-, or 5-mile radius of a burn pit or at all other locations during deployments in support of the operations in Iraq and Afghanistan. Possible exposure was assumed if deployment was to a location within a 2-, 3-, or 5-mile radius of a burn pit. In addition, cumulative days of exposure within a 2-, 3-, or 5-mile radius of a burn pit were assessed. Cumulative days of potential exposure to a burn pit was measured from 2003 through the follow-up survey assessment and categorized into quartiles in reference to those not exposed. Finally, exposure within a 2-, 3-, or 5-mile radius of a documented open-air burn pit was assessed by the specific campsite. If participants were deployed to multiple sites, they were categorized on the basis of the camp to which they were deployed with the longest exposure time.

Study Population

All analyses were restricted to Army and Air Force personnel because very few Navy and Marine Corps personnel were located within proximity to a documented burn pit in this sample. Of the

63,590 participants who completed both the 2004–2006 and 2007–2008 questionnaires, exclusions included those who affirmatively reported disease to all provider-diagnosed medical conditions, reported ever having lupus or rheumatoid arthritis prior to or on the 2004–2006 survey assessment, did not complete the outcome responses, or were missing any covariates of interest. In addition, participants were excluded if they were in the Navy or Marine Corps, never deployed between 2003 and 2007–2008 survey assessments, or experienced a first deployment or exposure to a documented burn pit after newly reporting either outcome.

Statistical Analysis

Multivariable logistic regression was performed for all analyses while adjusting for factors reported in the 2004–2006 survey that were potentially associated with lupus or rheumatoid arthritis and burn pit exposure. Model diagnostic tests were performed to assess multicollinearity, and potential confounders were evaluated if they changed the measure of association by more than 10%. The interaction between sex and proximity to a burn pit was also tested. Variables that were not confounders and were not significant in the model at $P < 0.05$ were removed using a backward manual reduction strategy to establish the final models. If a variable was neither confounding nor significant but had been consistently associated with lupus or rheumatoid arthritis in previous published literature, the variable was retained in the model. These variables included sex and birth year for the lupus model and sex, race/ethnicity, and smoking status for the rheumatoid arthritis model.^{35–37,43,44} Statistical analyses were performed using SAS version 9.2 (SAS Institute, Inc., Cary, NC).

Additional sensitivity analyses were performed to further investigate the associations between newly reported lupus and rheumatoid arthritis and burn pit exposure. The confirmed cases for both lupus and rheumatoid arthritis were assessed similar to the original self-reported models among active-duty members that had not separated from the service as of the 2007–2008 survey date. Proximity to a burn pit was additionally assessed while adjusting for separation from the military as of the 2007–2008 survey assessment. Furthermore, the Defense Manpower Data Center provided additional data for deployers to Camp Arifjan, Kuwait, which does not contain a documented open-air burn pit. A subset of other deployed was categorized as Arifjan deployed if they were deployed to Camp Arifjan longer than any other location in support of the operations in Iraq and Afghanistan. Because of the small sample, this sensitivity analysis was only performed for the rheumatoid arthritis model. Finally, members previously excluded from the first enrollment who newly reported either outcome on the 2004–2006 questionnaire were included to evaluate the impact of these additional cases in relation to proximity to a burn pit.

RESULTS

After exclusions, there were nearly 20,000 deployed Millennium Cohort members for the lupus ($n = 19,157$) and rheumatoid arthritis ($n = 18,848$) study populations. This included 3201 and 3145 participants from the respective lupus and rheumatoid arthritis study populations identified with at least one deployment to an area within a 3-mile radius of a documented open-air burn pit. Those deployed and meeting criteria for burn pit exposure were proportionately more likely to be younger, less educated, in the Army, and serving on active duty status than those not exposed (Table 1). The mean years from the initial date of exposure to the 2007–2008 survey date was 1.3 years (standard deviation, 0.9; minimum, 0.4; maximum, 2.8) for those reporting lupus and 1.7 years (standard deviation, 1.0; minimum, 0.05; maximum, 3.7) for those reporting rheumatoid arthritis. In addition, the cumulative incidence over the average 2.8 years of follow-up for lupus and rheumatoid arthritis

TABLE 1. Baseline Characteristics of Deployed Army and Air Force Millennium Cohort Participants in Relation to Burn Pit Exposure Within a 3-Mile Radius (2004–2008)

Characteristics	Lupus Study Population				Rheumatoid Arthritis Study Population			
	Other Deployment*† (n = 15,956)		Exposed Deployment (n = 3,201)		Other Deployment*‡ (n = 15,703)		Exposed Deployment (n = 3,145)	
	n	%	n	%	n	%	n	%
Newly reported disease								
No	15,941	99.9	3,195	99.8	15,510	98.8	3,104	98.7
Yes	15	0.1	6	0.2	193	1.2	41	1.3
Sex								
Male	12,087	75.8	2,371	74.1	11,879	75.6	2,326	74.0
Female	3,869	24.2	830	25.9	3,824	24.4	819	26.0
Birth year								
Before 1960	1,968	12.3	195	6.1	1,896	12.1	184	5.9
1960–1969	4,941	31.0	925	28.9	4,823	30.7	891	28.3
1970–1979	5,468	34.3	1,220	38.1	5,418	34.5	1,207	38.4
1980 and later	3,579	22.4	861	26.9	3,566	22.7	863	27.4
Race/ethnicity								
Non-Hispanic white	11,306	70.9	2,162	67.5	11,154	71.0	2,124	67.5
Non-Hispanic black	1,643	10.3	386	12.1	1,598	10.2	377	12.0
Hispanic	1,080	6.8	239	7.5	1,063	6.8	237	7.5
Other	1,927	12.1	414	12.9	1,888	12.0	407	12.9
Education								
High school or less	9,592	60.1	2,124	66.4	9,453	60.2	2,090	66.5
Some college	1,391	8.7	282	8.8	1,347	8.6	274	8.7
Bachelor's degree or higher	4,973	31.2	795	24.8	4,903	31.2	781	24.8
Marital status								
Married	9,443	59.2	1,807	56.5	9,254	58.9	1,761	56.0
Not married	6,513	40.8	1,394	43.5	6,449	41.1	1,384	44.0
Service component								
Active duty	7,788	48.8	1,734	54.2	7,650	48.7	1,703	54.1
Reserve/National Guard	8,168	51.2	1,467	45.8	8,053	51.3	1,442	45.9
Military pay grade								
Enlisted	11,697	73.3	2,434	76.0	11,498	73.2	2,388	75.9
Officer	4,259	26.7	767	24.0	4,205	26.8	757	24.1
Service branch								
Army	10,457	65.5	2,334	72.9	10,245	65.2	2,293	72.9
Air Force	5,499	34.5	867	27.1	5,458	34.8	852	27.1
Occupation								
Combat specialist	3,595	22.5	599	18.7	3,555	22.6	589	18.7
Health care specialist	1,330	8.3	327	10.2	1,319	8.4	321	10.2
Functional support	2,853	17.9	515	16.1	2,782	17.7	500	15.9
Electrical/mechanical	2,037	12.8	543	17.0	2,001	12.7	538	17.1
Service support	1,928	12.1	336	10.5	1,891	12.0	329	10.5
Other	4,213	26.4	881	27.5	4,155	26.5	868	27.6
Body mass index (kg/m ²)								
Normal/underweight (<25)	6,544	41.0	1,312	41.0	6,479	41.3	1,311	41.7
Overweight (25 to <30)	7,645	47.9	1,570	49.0	7,510	47.8	1,525	48.5
Obese (≥30)	1,767	11.1	319	10.0	1,714	10.9	309	9.8
Smoking status								
Nonsmoker	9,346	58.6	1,847	57.7	9,220	58.7	1,813	57.6
Past smoker	3,790	23.8	739	23.1	3,717	23.7	729	23.2
Current smoker	2,820	17.7	615	19.2	2,766	17.6	603	19.2

(Continued)

TABLE 1. (Continued)

Characteristics	Lupus Study Population				Rheumatoid Arthritis Study Population			
	Other Deployment*† (n = 15,956)		Exposed Deployment (n = 3,201)		Other Deployment*‡ (n = 15,703)		Exposed Deployment (n = 3,145)	
	n	%	n	%	n	%	n	%
Alcohol misuse								
No	13,166	82.5	2,637	82.4	12,967	82.6	2,587	82.3
Yes	2,790	17.5	564	17.6	2,736	17.4	558	17.7
Mental component score								
>75th percentile	3,936	24.7	768	24.0	3,875	24.7	746	23.7
>50th to 75th percentile	3,896	24.4	798	24.9	3,863	24.6	790	25.1
>25th to 50th percentile	3,924	24.6	812	25.4	3,856	24.6	789	25.1
0 to 25th percentile	4,200	26.3	823	25.7	4,109	26.2	820	26.1
Physical component score								
>75th percentile	3,853	24.1	834	26.1	3,815	24.3	812	25.8
>50th to 75th percentile	3,878	24.3	786	24.6	3,813	24.3	781	24.8
>25th to 50th percentile	3,974	24.9	798	24.9	3,911	24.9	779	24.8
0 to 25th percentile	4,251	26.6	783	24.5	4,164	26.5	773	24.6
Chemical/biological warfare agents								
No	15,385	96.4	3,118	97.4	15,156	96.5	3,063	97.4
Yes, 1 or more times	571	3.6	83	2.6	547	3.5	82	2.6
Hazards requiring personal protective equipment								
No	6,193	38.8	1,332	41.6	6,142	39.1	1,306	41.5
Yes	9,329	58.5	1,793	56.0	9,143	58.2	1,765	56.1
Don't know	434	2.7	76	2.4	418	2.7	74	2.4
Routine skin contact with paint, solvents, substances								
No	11,385	71.4	2,282	71.3	11,254	71.7	2,246	71.4
Yes	3,621	22.7	757	23.6	3,519	22.4	741	23.6
Don't know	950	6.0	162	5.1	930	5.9	158	5.0
Microwaves (excluding microwave ovens)								
No	11,928	74.8	2,453	76.6	11,790	75.1	2,407	76.5
Yes	2,166	13.6	450	14.1	2,098	13.4	449	14.3
Don't know	1,862	11.7	298	9.3	1,815	11.6	289	9.2
Pesticides (creams, sprays, uniform treatments)								
No	7,991	50.1	1,702	53.2	7,921	50.4	1,675	53.3
Yes	6,828	42.8	1,302	40.7	6,669	42.5	1,275	40.5
Don't know	1,137	7.1	197	6.2	1,113	7.1	195	6.2
Pesticides (environment, living facilities)								
No	8,180	51.3	1,791	56.0	8,120	51.7	1,758	55.9
Yes	5,433	34.0	1,006	31.4	5,278	33.6	981	31.2
Don't know	2,343	14.7	404	12.6	2,305	14.7	406	12.9

*Deployment in support of the operations in Iraq and Afghanistan not within a 3-mile radius of a documented open-air burn pit.

†For the lupus study population, all characteristics were statistically significant ($P < 0.05$) in univariate analyses except lupus; body mass index; smoking status; alcohol misuse; mental component score; and routine skin contact with paint, solvents, substances.

‡For the rheumatoid arthritis study population, all characteristics were statistically significant ($P < 0.05$) in univariate analyses except rheumatoid arthritis; body mass index; smoking status; alcohol misuse; mental component score; physical component score; and routine skin contact with paint, solvents, substances.

was 0.24 per 1000 person-years and 2.68 per 1000 person-years, respectively.

Because of insufficient sample size, analyses for the lupus models within a 2-mile radius of a documented burn pit were not conducted. For the final lupus model within a 3-mile radius of a burn pit, sex, birth year, education, marital status, service component, military pay grade, service branch, occupation, body mass index, smoking status, alcohol misuse, mental and physical component scores, and exposure to occupational hazards requiring personal protective equipment, chemical or biological warfare agents, microwaves, and environmental and topical pesticides were not significant predictors ($P \geq 0.05$) and did not confound the results. These covariates, except for sex and birth year, were removed from the model. After adjusting for sex, birth year, race/ethnicity, and routine skin contact with paints, solvents, or substances, we found that in the combined three-camp burn pit analysis, exposure within a 3-mile proximity to a burn pit ($P = 0.083$) and cumulative days exposed within a 3-mile radius of a burn pit ($P = 0.168$) were not significantly associated with newly reported lupus compared with those not exposed (Tables 2 and 3). However, those deployed to JBB were more than three times more likely to newly report lupus than those not within a 3-mile proximity to a burn pit (odds ratio, 3.51; 95% confidence interval, 1.56 to 8.51); however, this finding was based on only two cases. Analyses conducted within a 5-mile proximity to a burn pit were similar to those within 3 miles because of minimal differences in the number of exposed participants between the 3-mile ($n = 3201$) and 5-mile ($n = 3225$) proximities of a documented open-air burn pit.

Similar to the lupus model, insufficient sample size prevented the rheumatoid arthritis analyses from being performed for the 2-mile

radius of a documented burn pit. For the final rheumatoid arthritis model within a 3-mile radius of a burn pit, sex; race/ethnicity; education; occupation; body mass index; smoking status; alcohol misuse; exposure to occupational hazards requiring personal protective equipment; skin contact with paints, solvents, or substances; exposure to chemical or biological warfare agents; and exposure to environmental and topical pesticides were not significant predictors ($P \geq 0.05$) and did not confound the results. These covariates were removed from the model, with the exception of sex, race/ethnicity, and smoking status. After adjusting for sex, birth year, race/ethnicity, marital status, service component, military pay grade, service branch, smoking status, mental and physical component scores, and exposure to microwaves, in the combined three-camp burn pit analysis, proximity to a burn pit ($P = 0.369$), cumulative days within a 3-mile radius of a burn pit ($P = 0.181$), and proximity by site ($P = 0.343$) were not significantly associated with newly reported rheumatoid arthritis compared with deployed who were not exposed within a 3-mile proximity to a burn pit (Tables 4 and 5). However, exposure to the burn pit for 132 to 211 days was associated with an increased risk of newly reported rheumatoid arthritis compared with those unexposed, whereas exposure greater than 211 days was not. With minimal differences in the number of participants exposed between the 3-mile ($n = 3145$) and 5-mile ($n = 3169$) radii, the results for analyses conducted for the 5-mile proximity to a burn pit were similar to those exposed within 3 miles.

The interaction between proximity to a burn pit and sex was not statistically significant for newly reported lupus or rheumatoid arthritis; therefore, the analyses were not stratified. In addition, the electronic medical records review confirmed 2 of the 10 (20.0%)

TABLE 2. Odds of Newly Reported Lupus Among Deployers in Relation to a 3-Mile Proximity to a Burn Pit, 2004–2008

Covariates	All Cohort Cases ($n = 21$)						Confirmed Cases* ($n = 2$)				
	n^{\dagger}	% [†]	OR	95% CI	P	AOR	95% CI	P	AOR	95% CI	P
Deployment					0.114			0.083			0.677
Other deployed‡	15	71.4	1.00§			1.00§			1.00§		
Exposed deployed	6	28.6	2.09	0.84–5.23		2.11	0.91–4.92		0.66	0.09–4.73	
Sex					0.131			0.090			0.032
Male	13	61.9	1.00§			1.00§			1.00§		
Female	8	38.1	1.94	0.82–4.58		2.06	0.89–4.75		6.81	1.18–39.13	
Birth year					0.747			0.487			0.530
Before 1960	3	14.3	1.00§			1.00§			1.00§		
1960–1969	6	28.6	0.69	0.19–2.51		0.54	0.16–1.84		0.12	0.01–2.32	
1970–1979	9	42.9	0.88	0.26–2.99		0.67	0.21–2.13		0.23	0.02–2.77	
1980 and later	3	14.3	0.49	0.11–2.15		0.34	0.08–1.41		0.34	0.03–4.27	
Race/ethnicity					0.013			0.011			0.086
Non-Hispanic white	10	47.6	1.00§			1.00§			1.00§		
Non-Hispanic black	7	33.3	4.75	1.86–12.15		4.63	1.87–11.48		16.23	1.73–152.49	
Hispanic	1	4.8	1.46	0.26–8.08		1.41	0.29–6.94		6.62	0.39–111.43	
Other	3	14.3	1.92	0.57–6.44		2.07	0.66–6.49		4.13	0.25–69.25	
Routine skin contact with paint, solvents, substances					0.047			0.006			0.543
No	10	47.6	1.00§			1.00§			1.00§		
Yes	9	42.9	2.83	1.18–6.81		3.67	1.60–8.42		1.60	0.22–11.95	
Don't know	2	9.5	2.93	0.74–11.66		3.44	0.96–12.33		3.28	0.38–28.68	

All models are adjusted for sex, birth year, race/ethnicity, and routine skin contact with paints, solvents, or substances; Firth's method was used. AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

*Confirmed cases model is among active-duty, nonseparated participants; Firth's method was used.

†Frequencies and percentages of newly reported Cohort cases.

‡Deployment in support of the operations in Iraq and Afghanistan not within a 3-mile radius of a documented open-air burn pit.

§Indicates reference category.

TABLE 3. Odds of Newly Reported Lupus Among Deployers in Relation to a 3-Mile Proximity to a Burn Pit by Cumulative Days and Campsite, 2004–2008

	All Cohort Cases (n = 21)							Confirmed Cases* (n = 2)			
	n†	%†	OR	95% CI	P	AOR	95% CI	P	AOR	95% CI	P
Exposed days								0.168			
0‡	15	71.4	1.00§								0.733
1–55	1	4.8	1.93	0.36–10.31		1.91	0.40–9.05		3.23	0.37–28.32	
56–131	1	4.8	1.93	0.36–10.34		2.00	0.43–9.45		2.84	0.29–28.02	
132–211	2	9.5	3.20	0.84–12.22		3.37	0.97–11.71		1.89	0.19–18.76	
>211	2	9.5	3.24	0.85–12.36		3.11	0.90–10.72		2.42	0.26–22.72	
Campsite								0.003			
No exposure‡	15	71.4	1.00§								0.668
JBB	6	28.6	3.51	1.40–8.78		3.65	1.56–8.51		1.15	0.13–10.12	
Taji	0	0.0									
Speicher	0	0.0									

All models are adjusted for sex, birth year, race/ethnicity, and routine skin contact with paints, solvents, or substances; Firth's method was used. AOR, adjusted odds ratio; CI, confidence interval; JBB, Joint Base Balad; OR, odds ratio.

*Confirmed cases model is among active-duty, nonseparated participants; Firth's method was used.

†Frequencies and percentages of newly reported Cohort cases.

‡Deployment in support of the operations in Iraq and Afghanistan not within proximity to a documented open-air burn pit.

§Indicates reference category.

self-reported lupus cases and 10 of the 98 (10.2%) self-reported rheumatoid arthritis cases among active-duty deployers. The clinical records review, when available, verified similar percentages of the self-reported cases. Among confirmed cases, burn pit exposure was not significantly associated with newly reported lupus or rheumatoid arthritis. Also, the models adjusting for separation, in addition to all other covariates, resulted in similar findings for those exposed compared with other deployed (lupus, $P = 0.069$; rheumatoid arthritis, $P = 0.187$). After adjusting, proximity by site, including Arifjan, was not significantly associated with an increased risk of rheumatoid arthritis compared with those not exposed ($P = 0.357$). Also, there was no significant association for JBB, Camp Taji, or Camp Speicher when compared with those deployed to Arifjan. Finally, in addition to the original cases, including the 2004–2006 newly reported outcomes increased the number of cases for lupus by 6 and rheumatoid arthritis by 153. After adjusting, proximity to a burn pit was not significantly associated with newly reported lupus or rheumatoid arthritis.

DISCUSSION

Understanding the potential health effects from unique environmental exposures that service members experience during deployment has gained much attention, particularly with smoke from open-air burn pits in Iraq and Afghanistan. Furthermore, the US Army Public Health Command has noted that the burn pits in these locations may contain a wide range of toxins, many of which have been associated with autoimmune disorders in previous literature.^{5,12–15,26,29,30,32,34} In light of these concerns, this study prospectively assessed newly reported lupus and rheumatoid arthritis in relation to a 3- and 5-mile proximity to a documented open-air burn pit at three different sites among deployed Millennium Cohort participants. The current results show that in the combined three-camp burn pit analysis, when compared with those not within a 3- or 5-mile proximity, there was no significant increase in risk for newly reported lupus or rheumatoid arthritis in relation to proximity to a burn pit and cumulative days exposed. These findings were consistent with sensitivity analyses of electronic medical record-confirmed cases. Given the short period of follow-up available at this time for study participants, these analyses cannot ad-

dress any long-term consequences of burn pit exposure on disease risk.

Although there was no overall significantly increased risk, the elevated and statistically significant association between newly reported lupus and deployment within 3- and 5-mile radii of the burn pit at JBB may be of concern, even though the number of exposed cases was small ($n = 2$). Although this may be a spurious finding due to the many comparisons conducted in these analyses, there have been associations documented between some chemical and environmental exposures and risk for lupus in previous research.^{5,12–15,33} It is difficult to speculate on biological plausibility without knowing the exact composition and exposure dose of materials that were burned and present in inhalable fumes at the burn pits. The elevated risk between newly reported lupus and proximity to JBB was not supported by sensitivity analyses among the confirmed lupus cases and lends credence to the possibility that this finding may have been spurious. This relatively short-term follow-up finding, however, warrants further long-term study of personnel deployed to this camp site. In addition, there was a noteworthy association between increasing cumulative days exposed and newly reported lupus; however, a trend analysis was performed to test for a dose-response relationship but was not statistically significant ($P = 0.104$). There was also a slight association between those exposed for 132 to 211 days and newly reported rheumatoid arthritis. This may be due to chance because exposure longer than 211 days was not significantly associated, as would be expected if a dose-response relationship existed.

Among the sensitivity analyses performed, the electronic medical record review confirmed 2 of 10 lupus and 10 of 98 rheumatoid arthritis cases among active-duty, nonseparated participants. This confirmation was limited to reviewing the diagnoses among non-separated, active-duty personnel because Reservists and those who have separated likely received care outside the military health care system. In addition, the electronic medical records accessed may not have represented all cases for this subpopulation if care was sought outside of the military health system and not revealed to military providers.

The findings for the models adjusting for separation were similar to the models not adjusting for separation, which may be due to the low rate (9%) of separation from the service as of the 2007–2008

TABLE 4. Odds of Newly Reported Rheumatoid Arthritis Among Deployers in Relation to a 3-Mile Radius of a Burn Pit, 2004–2008

Covariates	All Cohort Cases (n = 234)							Confirmed Cases* (n = 10)			
	n†	%†	OR	95% CI	P	AOR	95% CI	P	AOR	95% CI	P
Deployment					0.688			0.369			0.218
Other deployment‡	193	82.5	1.00§			1.00§			1.00§		
Exposed deployment	41	17.5	1.07	0.77–1.50		1.17	0.83–1.64		1.81	0.71–4.64	
Sex					0.715			0.072			0.393
Male	179	76.5	1.00§			1.00§			1.00§		
Female	55	23.5	0.95	0.70–1.28		1.34	0.97–1.85		1.59	0.55–4.61	
Birth year					<0.001			<0.001			0.030
Before 1960	46	19.7	1.00§			1.00§			1.00§		
1960–1969	106	45.3	0.83	0.59–1.18		0.63	0.43–0.90		0.36	0.09–1.53	
1970–1979	63	26.9	0.42	0.29–0.62		0.30	0.20–0.46		0.14	0.03–0.68	
1980 and later	19	8.1	0.19	0.11–0.33		0.13	0.07–0.24		0.05	0.00–0.57	
Race/ethnicity					0.010			0.065			0.705
Non-Hispanic white	143	61.1	1.00§			1.00§			1.00§		
Non-Hispanic black	33	14.1	1.58	1.08–2.31		1.13	0.76–1.68		0.75	0.17–3.30	
Hispanic	24	10.3	1.76	1.14–2.71		1.54	0.99–2.39		2.06	0.51–8.25	
Other	34	14.5	1.40	0.96–2.03		1.61	1.05–2.45		1.17	0.30–4.58	
Marital status					<0.001			0.006			0.336
Married	181	77.4	1.00§			1.00§			1.00§		
Not married	53	22.7	0.41	0.30–0.56		0.62	0.44–0.87		0.54	0.15–1.91	
Service component					<0.001			0.001			0.172
Active duty	146	62.4	1.00§			1.00§			1.00§		
Reserve/National Guard	88	37.6	0.59	0.45–0.77		0.62	0.46–0.83		2.68	0.65–11.09	
Military pay grade					<0.001			<0.001			0.371
Enlisted	198	84.6	1.00§			1.00§			1.00§		
Officer	36	15.4	0.51	0.36–0.73		0.44	0.29–0.66		0.51	0.12–2.23	
Service branch					0.005			0.022			0.962
Army	176	75.2	1.00§			1.00§			1.00§		
Air Force	58	24.8	0.66	0.49–0.88		0.70	0.51–0.95		0.98	0.35–2.74	
Smoking status					0.094			0.955			0.758
Nonsmoker	121	51.7	1.00§			1.00§			1.00§		
Past smoker	65	27.8	1.34	0.99–1.82		1.05	0.77–1.43		0.90	0.30–2.72	
Current smoker	48	20.5	1.31	0.94–1.83		1.02	0.72–1.44		1.46	0.45–4.72	
Mental component score					0.023			0.023			0.086
>75th percentile	50	21.4	1.00§			1.00§			1.00§		
>50th to 75th percentile	50	21.4	0.99	0.67–1.47		1.17	0.79–1.72		0.80	0.23–2.75	
>25th to 50th percentile	52	22.2	1.04	0.70–1.53		1.26	0.85–1.85		2.12	0.76–5.95	
0 to 25th percentile	82	35.0	1.54	1.08–2.19		1.71	1.19–2.46		0.22	0.03–1.98	
Physical component score					<0.001			<0.001			0.037
>75th percentile	19	8.1	1.00§			1.00§			1.00§		
>50th to 75th percentile	31	13.3	1.63	0.93–2.87		1.60	0.91–2.80		0.86	0.05–15.56	
>25th to 50th percentile	52	22.2	2.68	1.59–4.51		2.27	1.35–3.81		8.36	0.99–70.72	
0 to 25th percentile	132	56.4	6.52	4.04–10.50		4.57	2.84–7.36		9.56	1.12–81.82	
Microwaves (excluding microwave ovens)					<0.001			0.006			0.976
No	144	61.5	1.00§			1.00§			1.00§		
Yes	50	21.4	1.97	1.42–2.72		1.64	1.18–2.27		0.88	0.24–3.22	
Don't know	40	17.1	1.91	1.34–2.71		1.42	1.00–2.03		1.05	0.28–4.01	

All models are adjusted for sex, birth year, race/ethnicity, marital status, service component, military pay grade, service branch, smoking status, mental and physical component scores, and exposure to microwaves. AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

*Confirmed cases model is among active-duty, nonseparated participants; Firth's method was used.

†Frequencies and percentages of newly reported Cohort cases.

‡Deployment in support of the operations in Iraq and Afghanistan not within a 3-mile radius of a documented open-air burn pit.

§Indicates reference category.

TABLE 5. Odds of Newly Reported Rheumatoid Arthritis Among Deployers in Relation to a 3-Mile Proximity to a Burn Pit by Cumulative Days and Campsite, 2004–2008

	All Cohort Cases (n = 234)							Confirmed Cases* (n = 10)			
	n†	%†	OR	95% CI	P	AOR	95% CI	P	AOR	95% CI	P
Exposed days								0.181			
0‡	193	82.5	1.00§			1.00§			1.00§		
1–56	9	3.9	0.98	0.51–1.89		0.95	0.49–1.82		0.97	0.11–8.62	
57–131	11	4.7	1.23	0.67–2.23		1.47	0.81–2.68		3.21	0.81–12.73	
132–211	14	6.0	1.42	0.81–2.47		1.76	1.02–3.02		2.93	0.75–11.39	
>211	7	3.0	0.80	0.38–1.66		0.78	0.38–1.62		2.95	0.76–11.51	
Campsite								0.343			
No exposure‡	193	80.3	1.00§			1.00§			1.00§		
JBB	26	10.1	1.15	0.76–1.73		1.37	0.91–2.06		2.69	0.91–7.92	
Taji	9	3.9	1.44	0.75–2.78		1.24	0.64–2.41		2.86	0.71–11.56	
Speicher	6	2.6	0.72	0.33–1.58		0.74	0.34–1.63		0.89	0.10–7.94	

All models are adjusted for sex, birth year, race/ethnicity, marital status, service component, military pay grade, service branch, smoking status, mental and physical component scores, and exposure to microwaves. AOR, adjusted odds ratio; CI, confidence interval; JBB, Joint Base Balad; OR, odds ratio.

*Confirmed cases model is among active-duty, nonseparated participants; Firth's method was used.

†Frequencies and percentages of newly reported Cohort cases.

‡Deployment in support of the operations in Iraq and Afghanistan not within proximity to a documented open-air burn pit.

§Indicates reference category.

survey assessment. Furthermore, adding Camp Arifjan to the sensitivity analysis was valuable because of its location in a geographic region with meteorological conditions similar to JBB, Camp Taji, and Camp Speicher; however, this camp has its waste transported out of the area for disposal. Because there were no newly reported cases of lupus at Camp Arifjan, this analysis was only investigated for newly reported rheumatoid arthritis. Finally, the similar results from including the 2004–2006 newly reported cases ensured that the original models were robust. All sensitivity analyses were reassuring, with no significant associations between proximity to a burn pit and lupus and rheumatoid arthritis.

The crude incidence rates for the self-reported lupus (0.24 per 1000 person-years) and rheumatoid arthritis (2.68 per 1000 person-years) cases are higher than documented for the general US population (systemic lupus erythematosus, 0.02 to 0.08 per 1000 person-years; rheumatoid arthritis, 0.24 to 0.68 per 1000 person-years).^{43–47} However, the incidence rates among the confirmed cases for lupus (0.05 per 1000 person-years) and rheumatoid arthritis (0.23 per 1000 person-years) were within the reported ranges for the general population. It is difficult to compare the rates in this study with the US population because deployed Army and Air Force personnel may have been exposed to unique environmental and occupational risk factors not typically experienced in the general population. However, it is possible for these analyses to include some misclassification of both outcomes on the basis of self-report or electronic medical records review. Participants reporting lupus may have been diagnosed with any form of lupus and not systemic lupus erythematosus specifically because of the questionnaire not specifying which type of lupus was to be reported. Similarly, the questionnaire did not provide a description for rheumatoid arthritis and those with any arthritis, including the more common osteoarthritis, may have mistakenly endorsed this diagnosis.

Although the etiologies of lupus and rheumatoid arthritis are unknown, certain exposures known as xenobiotics (environmental contaminants and pharmacological agents) have been of interest recently as possible causes. Xenobiotics may impact the immune system in several different ways including, but not limited to, altering the regulation of autoreactive T cells and autoantibody production and

secretion of pro- and anti-inflammatory cytokines.^{5,15} These pathway impediments may ultimately lead to immune-enhancement causing chronic inflammation and tissue and organ damage.^{5,15,37} Further research on this class of exposures specifically and the constituents of burn pit smoke in particular are needed to better understand their possible roles in disease pathogenesis.

This study has several limitations, some of which have already been described. The current analyses used self-reported data from the Millennium Cohort questionnaire, which, by its nature, may contain biases; however, possible biases in these data were previously investigated, suggesting a representative cohort of US military personnel who report reliable data, with responses unaffected by the participant's health status prior to enrollment.^{38,40,48–56} Because of the large sample size and population-based design, conducting clinical examinations to confirm self-reported diagnoses was not feasible. Other risk factors were also not ascertainable such as genetic factors, family history, medications used, or exposure to silica dust, making it difficult to thoroughly examine all possible exposures for these diseases. In addition, lupus and rheumatoid arthritis are rare outcomes, resulting in few newly reported cases occurring during the average 2.8 years of follow-up. As a result, the precision of the estimates was low. Also, the induction period for these diseases between time of exposure and onset of illness is still under investigation and may be longer than the average follow-up duration in this analysis. This problem will likely be mitigated by additional follow-up of this cohort and an accumulating number of subsequent cases and years of follow-up that will permit more precise estimates of associations. By not adjusting the α level for significance in this study for multiple comparisons, the probability of any observed statistically significant difference being a result of chance alone was higher than when such an adjustment had been performed.

Another important limitation was that this study used data from documented burn pits at three camps only, and we were not able to assess burn pit exposure over the entire theater of operation. The burn pit data only included those deployed within 2-, 3-, and 5-mile radii of a documented open-air burn pit from 2003–2008 and do not allow for granularity of varied exposure levels at various sites or exposures prior to 2003. Furthermore, associations with a

burn pit site may not be entirely attributed to that particular burn pit because participants were categorized according to the longest exposure recorded. In addition, we were not able to assess and account for the direction of the smoke plume during burning operations, density of the plume, and types of materials burned at the pit sites. For these reasons, exposure misclassification may bias these results in either direction on the basis of random or nonrandom misclassification of exposure.²² Outside of occupation, we were unable to capture reasons for proximity to a burn pit. Some factors may include specific occupational duties and location of living quarters, though these were not measured in the current analysis. Finally, these analyses did not take into account the many other exposures found in theater, such as exposure from particulates, fuel, or those related to specific occupations, unless these were captured in our questionnaire.

Despite these limitations, our study has several unique strengths. This is the first study to prospectively investigate whether deployment-specific exposures are associated with newly reported, provider-diagnosed lupus and rheumatoid arthritis, while also being able to adjust for numerous potential confounders, including negative health behaviors, which may be associated with the development of these conditions. In addition, the prospective design of the Millennium Cohort Study allowed for assessment at baseline and follow-up of the same individuals. Also, given this study design, exposure assessment was not susceptible to recall bias. Finally, the large sample size representing both men and women, active duty, Reserve and National Guard personnel, and all branches of the service—although only Army and Air Force services were analyzed in this study—enhanced statistical power for assessing exposure–disease associations.

In conclusion, these results suggest no overall elevated risk of self-reported lupus or rheumatoid arthritis for those deployed within 3- and 5-mile radius of the combined three documented open-air burn pits investigated in these analyses, although exposure at JBB was individually associated with self-reported lupus. This study should be considered an important first look into immune-mediated response health concerns potentially associated with smoke exposure from open-air burn pits. Although these analyses did not find strong and consistent signals of effect for this exposure in Army and Air Force personnel at the population level, there may be specific subgroups of these deployed personnel with extensive exposure that may not have been identified. Further research, including additional follow-up of those deployed to JBB and documented burn pit sites integrating meteorological wind data and other in-theater exposures, should be conducted. As data collection proceeds in this cohort and additional exposure data become available, longitudinal analyses should be performed to further investigate the long-term development of lupus and rheumatoid arthritis in relation to deployment and associated exposures.

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REPORT DOCUMENTATION PAGE

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Background

Recently, there has been concern that service members deploying in support of the current operations in Iraq and Afghanistan may have higher odds of developing chronic diseases, such as lupus or rheumatoid arthritis, as a result of environmental and occupational exposures that have been associated with these diseases in the general US population. One such exposure garnering much attention from media and veterans groups suggest smoke from open-air burning of trash and other waste in theater is contributing to widespread illness.

Methods

Of the 63,590 participants who completed both the 2004–2006 and 2007–2008 questionnaires, exclusions included those who affirmatively reported disease to all provider-diagnosed medical conditions, reported ever having lupus or rheumatoid arthritis prior to or on the 2004–2006 survey assessment, did not complete the outcome responses, were in the Navy or Marine Corps, never deployed between 2003 and 2007–2008 survey assessments, experienced a first deployment or exposure to a documented burn pit after newly reporting either outcome, or were missing any covariates of interest.

Results

3201 and 3145 participants from the respective lupus and rheumatoid arthritis study populations identified with at least one deployment to an area within a 3-mile radius of a documented open-air burn pit. After adjustment, proximity to a documented 3-mile burn pit was not significantly associated with rheumatoid arthritis or lupus in general.

Conclusions

Results indicate deployers exposed to documented burn pits in the combined three-camp analysis were not at an elevated risk of lupus or rheumatoid arthritis.

15. SUBJECT TERMS

Burn pits, environmental exposure, air pollutants, autoimmune, combat, veterans

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